Clinical outcomes among persons living with HIV (PLWH) initiating dolutegravir-based vs. other recommended regimens in clinical care from the Centers for AIDS Research Network of Integrated Systems (CNICS)

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BACKGROUND

- Much of the data on clinical outcomes with integrase strand transfer inhibitors (INSTI) are from clinical trials rather than clinical care settings
- Even less is known about recently approved INSTI: Dolutegravir (DTG)
- We conducted this study to compare outcomes among people living with HIV (PLWH) who initiated DTG-based vs. other guideline recommended regimens in real-world clinical care settings across the U.S.

Figure 1. Centers for AIDS Research Network of Integrated Clinical Systems (CNICS) Cohort Map

METHODS

- Treatment-naïve PLWH from 8 CNICS sites who started a recommended regimen between 8/2013-3/2017 were included (Figure 1)
- We compared DTG vs. other INSTI, vs. darunavir-based (DRV) regimens included in contemporary guidelines for initiating ART
- We examined the proportion who:
  - remained on initial regimen
  - switched regimen
  - or discontinued regimens, and
  - who experienced viral failure (VF) defined as a viral load of >400 copies/mL[3] 6 months after initiation
- We used Cox models adjusting for age, sex, race/ethnicity, hepatitis B, hepatitis C, tuberculosis, HIV risk factor, CD4 count, days since last HIV viral load, and site
- We repeated analyses among those initiating these same recommend regimens but were not ART naïve at initiation

RESULTS

- Among 1373 treatment-naïve PLWH who initiated a recommended regimen
  - mean age was 35-38 by regimen
  - 35-38% were white (Table 1),
  - the percentage who remained on DTG-based regimens was similar to other INSTI or DRV-based regimens (69% vs. 64%; 69%) (Table 2)
  - the percentage who switched regimens was similar for DTG-based regimens vs. other INSTI or DRV-based regimens (17% vs. 13%; 18%)
  - however, 32% of those on DTG who switched regimens changed to another DTG-based recommended regimen (Triumeq) suggesting regimen simplification rather than intolerance
  - The proportion who experienced VF was lower for DTG-based regimens (6% vs. 12%; 27%)
- Among 6757 treatment experienced PLWH who initiated a recommended regimen
  - the mean age across regimens was 43-48, 76-78% were women (Table 1)
  - 46-67% remained on their regimens
  - the percentage on DTG who experienced VL failure was lower than the percentage on DRV-based regimens (Table 2)
- The adjusted hazard ratio (aHR) for time to VF for DTG-based vs. DRV-based was 0.37 (95% CI: 0.16-0.86) among treatment naïve PLWH and 0.60 (95% CI:0.43-0.84) among treatment experienced PLWH. Most other associations in adjusted Cox models were non-significant

Table 1. Demographic and clinical characteristics at ART initiation by past treatment status and regimen

	Treatment-Naïve Patients (N = 1373)			Treatment-Experienced Patients (N = 6757)		
	Regimen			Regimen		
Characteristic	**DTG-Based Preferred[a]**	**Other INSTI**	**Darunavir Based**	**DTG-Based Preferred**	**Other INSTI**	**Darunavir Based**
Age at study entry (years)						
Mean (SD)	38 (13)	35 (11)	36 (9)	48 (11)	43 (11)	43 (10)
Sex, %						
Male	82	88	98	78	78	76
Female	18	12	2	22	22)	24
Race/ethnicity, %						
White	38	35	36	46	39	29
Black	45	48	38	41	46	60
Hispanic	9	9	17	10	11	8
Other/missing	8	7	9	3	4	3
Time in care before starting regimen (years)						
Mean (SD)	1.0 (2.7)	0.6 (2.0)	0.9 (2.2)	7.8 (5.7)	6.0 (5.4)	6.1 (5.4)
CD4 count at treatment initiation (cells/mm^3)						
Mean (SD)	370 (255)	399 (277)	384 (261)	595 (347)	564 (324)	428 (295)

DTG = dolutegravir; INSTI = integrase strand transfer inhibitor; SD = standard deviation.
[a] This includes Dolutegravir/abacavir/emtricitabine and Dolutegravir/tenofovir/emtricitabine

Table 2. Outcomes by past treatment status and regimen

	Treatment-Naïve Patients (N = 1373)			Treatment-Experienced Patients (N = 6757)		
	Regimen			Regimen		
Characteristic	**DTG-Based Preferred[a]**	**Other INSTI**	**Darunavir Based**	**DTG-Based Preferred**	**Other INSTI**	**Darunavir Based**
Duration of followup (days), mean (SD)	522 (349)	662 (405)	730 (506)	530 (348)	565 (391)	547 (405)
Experienced virologic failure, n (%)	28 (6)	93 (12)	23 (27)	115 (5)	152 (9)	75 (20)
Died, n (%)	0 (0)	4 (1)	3 (4)	30 (1)	13 (1)	7 (2)
Remained on index treatment, n (%)	303 (69)	505 (64)	59 (69)	1479 (67)	997 (62)	170 (46)
Switched from index treatment, n (%)	74 (17)	101 (13)	15 (18)	333 (15)	290 (18)	96 (26)

DTG = dolutegravir; INSTI = integrase strand transfer inhibitor; SD = standard deviation.
[a] This includes Dolutegravir/abacavir/emtricitabine and Dolutegravir/tenofovir/emtricitabine

DISCUSSION

- We limited to regimens starting after 8/13 to enhance comparability across regimens and ensure access to all the medications of interest to minimize bias
- Primary analyses were among those known to be ART naïve to minimize differences in PLWH who started each regimen

CONCLUSIONS

- The proportion of treatment-naive PLWH remaining on recommended DTG-based regimens was similar to other regimens but the proportion with VF was lower
- While switching regimens was common in all groups, individuals on DTG were more often 'switched' to another DTG-based regimen, usually for regimen simplification

ACKNOWLEDGMENTS

This study was possible due to funding from ViiV and the NIH